Symbolic Systems Technology

Using formal systems and reasoning tools to
• Understand how things work; why things don’t work
• Design, analyze, adapt complex systems

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Plan

- About formal systems, formal modeling
- Some examples
- Challenges & Opportunities
Complex systems -- a small sample

- Communicating processes
  - dissemination of messages/knowledge (routing protocols)
  - security protocols
  - business processes/regulations
- Collaborations
  - emergency response
  - surveillance
- Cellular systems
  - signaling (intra, inter) -- regulation, decision making
  - metabolism
  - resilience, fault tolerance
Modeling Step One

• What questions do you want the model answer?

• What can you observe/measure?

• What questions do you *really* want the model answer?

• What does that mean?

• Explain it to a computer!
What is a formal system?

- Language: to describe things and properties
- Semantics: thing satisfies property
- Reasoning principles: proving/disproving properties of things
- [Reflection: to model and reason about models and reasoning]
- Executable formal models (model train, airplane, ...)
  - System state: collections of entities (name, location, knowledge, resources..)
  - State transition rules
  - Execution: application of rules
  - Properties of states (P,Q) and executions (ϕ: P until Q, eventually P)
- Watch it run, poke it, analyze it
Symbolic analysis -- answering questions

- Forward collection -- upper bound on possible states
- Backward collection -- initial states leading to states of interest
- Search -- for state of interest
- Model checking -- do all executions satisfy $\phi$, find counter example
- Constraint solving -- steady state analysis
Rewriting Logic & Maude

- Rewriting logic is a simple logic designed to model concurrent and distributed systems,
  - System states described by equational theories, behavior described by local rules
- Maude is modeling environment based on rewriting logic, featuring
  - a high speed rewriting modulo axioms
  - built in search, model-checking, unification
  - reflection
Modeling Methodology

- Modeling Methodology
- Impact
- Rapid prototyping
- State space search
- $S = \Phi$
- Model checking
- Yearly Monthly Weekly Daily Monthly
- Database SQL
- Reports/alarms Logs
- E-mail Pager
- Fault Configuration Accounting Performance Security
- Resource monitoring
- Rapide prototyping
- State space search
Finding Bugs in Complex Systems

- AER/NCA active network reliable multicast protocol
  - Is the nominee (chosen responder) aware?
  - Do the agents come to agreement within time $t$?
  - Poor timer setting leads to bad behavior

- Secure service broker via proxies
  - Is the service from a trusted provider
  - Is it the requested service

- Security issues in IE (Meseguer et. al.)
  - found nine status bar types of spoofing attacks and four address bar spoofing attack types
More Applications

- Border Gateway Protocol Analysis (Anduo Wang, Boon Tau Loo, Andre Scedrov UPenn)
- Looping -- fail to find route
- Inconsistency -- intra vs inter

- Modeling Regulations for Clinical Trials (Andre Scedrov (UPenn), Vivek Nigam (Munich), ....
- Federal regulations, clinical protocol
- Events and obligations
- Runtime monitoring
- Situation aware plan generation
- Post trial inspection

Internet Routing Systems
Share connectivity information across ASes

- BGP: Border gateway protocol.
- iBGP within AS
- eBGP across AS

IGP: Interior Gateway Protocol.
Example: OSPF, RIP

Plan Generation
Execution Monitoring

FDA / Sponsor / P
Xtune
cross layer adaptation

Constraint refinement

A user resides in zone 2
Dependability Techniques for Instrumented Cyber-Physical Spaces

- Principles / techniques for infrastructure and data resilience
- Formal models and cross-layer tuning
- Middleware services
- Pervasive space testbed

Instrumented UCI Campus
Biology

- Pathway Logic
- Combining Pathways and Cheminformatics
- Diet Planning
The essence

- Formal models of experimental findings
- Executable models of biological processes
- Pathways (sets of biomolecules that function together) and regulation effects discovered by asking questions (answered by formal reasoning)

Sample models

- Mammalian intra cellular signaling
- Bacterial protease interactions
- TB mycolic acid synthesis
- Function of sleep
Datum query

Signaling response to Egf (AMK)

Predicates

Assay: Activation Assay

50 of 407 Results

Export all results to txt or csv

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Erks[Ab][IP IVKA(MBP)][32P-ATP] is increased Lps (times) [Expand]
- cells: mPECs in BMS
- times: 0 7+ 15+ 30 60 90 min
- partially reqs: IraK1 [K0]
- source: 10754329-Fig-3c

Erks[Ab][IP IVKA(Elk1)][32P-ATP] is increased Lps (30 min) [Expand]

Two ways to activate Erk
Protease interaction network (Gram Positive Bacteria) (Anupama)

What regulates a protease, what does it regulate

What happens if you knockout FtsH?

- initial states
- possible reachable states
- transition/rules
- consumed/produced
- enzymatic relation
Multiple synthesis routes

TB-mycolic-acid synthesis (Malabika)
A Hypothetical Model Pathway Relating State and Synaptic Plasticity

Wake state:
- unknown signal(s)
  - => phosphorylation of Rock1
  - => activation of Limk1
  - => phosphorylation of cofilin
  - => increase in polymerized actin
    (Phosphorylated cofilin is unable to depolymerize actin)

SWS:
- RhoDG11 binds Rhob-GDP (is not phosphorylated)
  - => Rock1, Limk1, and cofilin would not be phosphorylated and
  - => actin depolymerization
  - => decrease in synaptic weight
Diet planning for Ecoli (aka finding minimal nutrient sets)

- Metabolic network, transportables, and growth conditions, represented as constraints.
- Find all minimal nutrient set solutions
- OOPS there are ~8560
- Partition nutrients into equivalence classes (replacable)
- 19 sets with 12 classes
- Surprise! E.Coli can grow on cyanate (and several other novel nutrient sets).
Combining Cheminformatics and Pathway Analysis
Finding TB drug candidates
NIH STTR with Collaborative Drug Design (CDD)

- Identify essential genes/enzymes
- Select substrates of highly connected enzymes
- Generate pharmacophores (abstract model of metabolite)
- Look for matches in drug catalog
- Predicted 30 candidate drugs, tested 20, 3 had activity
- Phase II STTR submitted.
Challenges and Opportunities

- Cyberphysical Systems
- Communicating cellular processes
Networked cyber-physical systems

- Networked Cyber-Physical Systems (NCPS) consist of networked hard- and software components embedded in the physical world and interacting with it through sensors and actuators.

- Increasingly large numbers of heterogeneous and potentially resource-constrained and unreliable components

- Need to work in challenging environments with unreliable/intermittent connectivity

- Need to operate in the entire spectrum between autonomy and cooperation

- Decisions based on local knowledge and knowledge dissemination

- Opportunity: General principles and tools for building robust, effective NCPS using individual cyber-physical devices as building blocks.
Communicating Cellular Systems

- For example the immune system, or neuron system, or combination ...

- All the NCPS challenges are relevant to modeling and understanding how these systems work:
  
  - What are the right abstractions?
  
  - What are the essential rules/balances that ensure correct/robust operation?
    
    - What are the underlying distributed, reactive control principles
  
  - What makes learning and adaptation work (or not)?
Principles and Foundations for NCPS

• **Problem:** Current models are too abstract by not taking into account fundamental physical limitations and hence are not efficiently implementable or scalable

• Once explicitly represented, physical limitations can be overcome to some degree (e.g. probabilistically)

• Diversification, redundancy, and randomization can offset many physical limitations

• Distribution is a source of redundancy and diversification and can be turned from an obstacle into an advantage
Vision

• Bringing together the cyber and the physical

• New insights for design and modification
  
  • synthetic biosystems; training colonies to do useful things

• New coordination/control laws
  
  • new ways to control the immune system

• on-the-fly self-assembling/organizing systems
The end! (The beginning?)